

In the claims:

Please amend claims 12 and 43 as follows:

1. (Previously presented) A composition comprising a glycosylated interferon-beta-1a comprising the amino acid sequence set forth in SEQ ID NO: 25 coupled to a non-naturally-occurring polymer at an N-terminal end of said glycosylated interferon-beta-1a, said polymer comprising a polyalkylene glycol moiety.
2. (Previously presented) The composition of claim 1, wherein the polyalkylene moiety is coupled to the interferon-beta by way of a group selected from an aldehyde group, a maleimide group, a vinylsulfone group, a haloacetate group, plurality of histidine residues, a hydrazine group and an aminothiol group.
3. (Cancelled).
4. (Cancelled).
5. (Previously presented) The composition of claim 1, wherein the interferon-beta-1a of SEQ ID NO: 25 is an interferon -beta-1a fusion protein.
6. (Previously presented) The composition of claim 5, wherein the interferon -beta-1a fusion protein comprises a portion of an immunoglobulin molecule.
7. (Previously presented) A composition comprising a glycosylated interferon-beta-1a comprising the amino acid sequence set forth in SEQ ID NO: 26 coupled to a non-naturally-occurring polymer at the N-terminus of said glycosylated interferon-beta-1a, said polymer comprising a polyalkylene glycol moiety.
8. (Previously presented) A physiologically active interferon-beta composition comprising a physiologically active interferon-beta-1a comprising the amino acid sequence of SEQ ID NO: 25, coupled to a polymer comprising a polyalkylene glycol moiety, wherein the interferon -beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is an N- terminal end, wherein the physiologically active interferon -beta 1a and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta-1a in the physiologically active interferon -beta composition has an activity at least 2-fold greater relative to physiologically active interferon-beta-1b, when measured by an antiviral assay.
9. (Cancelled).
10. (Cancelled).
11. (Previously presented) The composition of claim 8, wherein the interferon-beta-1a is coupled to the polymer at a site by way of a glycan moiety of the interferon-beta-1a.

12. (Previously presented) The composition of claim 8, wherein the interferon-beta-1a is an interferon-beta-1a fusion protein.
13. (Previously presented) The composition of claim 12, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.
14. (Cancelled).
15. (Previously presented) A physiologically active interferon-beta composition comprising a physiologically active glycosylated interferon-beta-1a comprising the amino acid sequence of SEQ ID NO: 25 N-terminally coupled to a polymer comprising a polyalkylene glycol moiety, wherein the physiologically active interferon-beta-1a and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta 1a in the physiologically active interferon-beta composition has equal activity relative to physiologically active interferon-beta lacking said moiety, when measured by an antiviral assay.
16. (Cancelled).
17. (Cancelled).
18. (Previously presented) The composition of claim 15, wherein the interferon-beta is coupled to the polymer at a site by way of a glycan moiety on the interferon-beta.
19. (Previously presented) The composition of claim 15, wherein the interferon-beta-1a is an interferon beta fusion protein.
20. (Previously presented) The composition of claim 19, wherein the interferon beta fusion protein comprises a portion of an immunoglobulin molecule.
21. (Cancelled).
22. (Previously presented) A stable, aqueously soluble, conjugated interferon-beta-1a complex comprising a interferon-beta-1a comprising the amino acid sequence of SEQ ID NO: 25, N-terminally coupled to a polyethylene glycol moiety, wherein the interferon-beta-1a is coupled to the polyethylene glycol moiety by a labile bond, wherein the labile bond is cleavable by biochemical hydrolysis and/or protcolysis.
23. (Previously presented) A interferon-beta composition according to claims 1, 15 and 22, wherein the polymer has a molecular weight of from about 5 to 40 kilodaltons.
24. (Previously presented) A pharmaceutical composition comprising the interferon-beta composition of claim 23.

25. (Withdrawn) A method of treating a potential or developed condition or disease state in a mammalian subject with a interferon-beta 1a effective therefore, comprising administering to the subject an effective amount of an interferon-beta 1a composition comprising said interferon-beta 1a coupled to a polyethylene glycol moiety.
26. (Withdrawn) The method of claim 25, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is an N-terminal end.
27. (Withdrawn) The method of claim 25, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is at or near the C-terminal end.
28. (Withdrawn) The method of claim 25, wherein the interferon-beta-a1 is coupled to the polymer at a site by way of a glycan moiety on the interferon-beta-1a.
29. (Withdrawn) The method of claim 25, wherein the interferon-beta-1a is an interferon-beta-1a fusion protein.
30. (Withdrawn) The method of claim 29, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.
31. (Withdrawn) The methods of claims 25 and 29, wherein the interferon-beta-1a is a mutant interferon-beta-1a having a least one of the following properties: (a) the mutant has a higher antiviral activity than wild type interferon beta 1a, wherein the antiviral activity is measured by viral induced lysis of cells; (b) the mutant has, relative to wild type interferon-beta-1a, greater antiviral activity than antiproliferative activity; (c) the mutant binds interferon receptor but has, when compared to wild type interferon-beta-1a, lowered antiviral activity and lowered antiproliferative activity relative to its receptor binding activity.
32. (Withdrawn) A method of prolonging the activity of interferon-beta-1a in an in vivo or in vitro system, comprising coupling said interferon-beta-1a to a non-naturally-occurring polymer moiety to yield a coupled polymer-interferon-beta 1a composition, and introducing the coupled polymer-interferon-beta composition to the in vivo or in vitro system.
33. (Withdrawn) The method of claim 32, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is an N-terminal end.
34. (Withdrawn) The method of claim 32, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is at or near C-terminal end.
35. (Withdrawn) The method of claim 32, wherein the interferon-beta-1a is coupled to the polymer at a site by way of glycan moiety on the interferon-beta-1a.

36. (Withdrawn) The method of claim 32, wherein in the interferon-beta-1a is an interferon-beta-1a fusion protein.

37. (Withdrawn) The method of claim 36, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.

38. (Withdrawn) The method of claims 32 and 36, wherein the interferon-beta-1a is a mutant interferon-beta-1a having at least one of the following properties: (a) the mutant has a higher antiviral activity than wild type interferon beta 1a, wherein the antiviral activity is measured by viral induced lysis of cells; (b) the mutant has, relative to wild type interferon-beta-1a, greater antiviral activity than antiproliferative activity; (c) the mutant binds interferon receptor but has, when compared to wild type interferon-beta-1a, lowered antiviral activity and lowered antiproliferative activity to its receptor binding activity.

39. (Withdrawn) The method of claim 32, wherein the polymer comprises a polyalkylene glycol.

40. (Withdrawn) The method of inhibiting angiogenesis in a subject, comprising administering to a subject an effective amount of the composition of claim 23.

41. (Previously presented) The composition of claim 7, wherein the glycosylated interferon-beta-1a comprising the amino acid sequence set forth in SEQ ID NO: 26 is an interferon-beta-1a fusion protein.

42. (Previously presented) The composition of claim 41, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.

43. (**Currently amended**) A physiologically active interferon-beta composition comprising a physiologically active interferon-beta-1a comprising the amino acid sequence of SEQ ID NO: 26, coupled to a non-naturally-occurring polymer at the N-terminus of said glycosylated interferon-beta-1a, said polymer comprising a polyalkylene glycol moiety wherein the physiologically active interferon-beta-1a and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta-1a in the physiologically active interferon-beta composition has an activity at least 2-fold greater relative to physiologically active interferon-beta-1b, when measured by an antiviral assay.

44. (Previously presented) The composition of claim 43, wherein the interferon-beta-1a is an interferon-beta-1a fusion protein.

45. (Previously presented) The composition of claim 44, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.

46. (Currently amended) A physiologically active interferon-beta composition comprising a physiologically active glycosylated interferon-beta-1a, comprising the amino acid sequence of SEQ ID NO: ~~25~~ 26, N-terminally coupled to a polymer comprising a polyalkylene glycol moiety, wherein the physiologically active interferon-beta-1a and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta-1a in the physiologically active interferon-beta composition has equal activity relative to physiologically active interferon-beta lacking said moiety, when measured by an antiviral assay.

47. (Previously presented) The composition of claim 16, wherein the interferon-beta-1a is an interferon beta fusion protein.

48. (Previously presented) The composition of claim 47, wherein the interferon beta fusion protein comprises a portion of an immunoglobulin molecule.